Remarks

Claims 1-29 and 34-36 and 40-42 have been canceled without prejudice. Claim 30 is canceled herein. Therefore, claims 31-33, 37-39, and 43-51 are pending. Applicants respectfully acknowledge the allowability of claims 31-33, 37, and 44- 47. Applicants have amended claims 38 and 39 to change their dependency to allowed claim 45. Applicants have amended claim 48 as described below.

35 U.S.C. § 112, first paragraph

Claims 30, 38, 39, 43, and 48-51 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide written description to reasonably convey to one of skill in the art to make or use the invention.

Regarding the Examiner's rejection of claim 30, Applicants have canceled claim 30 herein. Applicants believe this rejection is now moot and respectfully request its withdrawal.

Regarding the rejection of claims 38, 43, and 50, the Examiner contends that the claims "encompass the inhibition of rejection in *any* species, while only rhesus monkey is disclosed, and *any* type of tissue or organ, while only skin and kidney are disclosed." Applicants previously amended claims 38 and 43 to recite "mismatched kidney transplants." Support for these amendments can be found at least on page 40, lines 5-7, where the use of immunotoxins as an adjunct to induce tolerance to mismatched kidney transplants is discussed. The Examiner further alleges that the disclosure is not adequate for the use of the claimed immunotoxin in the methods of inhibiting kidney transplantation rejection. Specifically, the Examiner has further stated that allegedly support only exists for "an adjunct for inducing tolerance in mismatched kidney transplantation. Applicants respectfully point out that Example 9 on page 40, lines 5-7 provides literal support for methods of inhibiting rejection of mismatched kidney transplants. Moreover, as noted previously and shown throughout Example 7 of the specification and in particular on page 31, lines 17-19 and page 32, lines 19-26, transplant rejection is inhibited by inducing tolerance to the transplanted tissue by depleting the T cell population ("[t]he present example demonstrates a 2 log kill of T cells in rhesus monkey lymph nodes that is also shown to produce prolongation of skin allograft rejection in monkeys"). It should be scientifically clear that the

disclosed mechanism (T cell depletion) that inhibits rejection in the case of mismatched kidney transplants and skin allografts would produce this result in any other transplantation contexts. Nevertheless, in an effort to further prosecution, Applicants have amended claims 38, 43, and 50 to recite "by inducing tolerance to the mismatched kidney transplant." Support for this amendment can be found at least on page 40, lines 5-8 of the specification. Applicants believe this amendment raises no new issues as this support and these limitations have been previously considered.

As the Examiner is also focusing on the use of the immunotoxin FN18-CRM9 to induce tolerance to mismatched kidney transplants, Applicants point out, as indicated on page 27, lines 32-36 and page 39, line 35 through page 40 line 7 that FN18-CRM9 is the rhesus monkey analog of UCHT1-CRM9. FN18-CRM9 was used to show efficacy in reducing T cell count in the closest model available to humans. Applicants respectfully remind the Examiner that the description of using FN18-CRM9 to inhibit mismatched kidney transplant rejection is provided in the context description of methods for treating medical problems using UCHT1-CRM9. Thus, the use of the immunotoxin in humans to inhibit the rejection of kidney transplants was clearly contemplated and in Applicants' possession.

Furthermore, because CRM9 is a full-length toxin moiety and, as shown on page 40, lines 9-32, and the efficacy of a full-length toxin would be inhibited by pre-existing anti-diphtheria toxin antibodies in humans immunized against diphtheria, a truncation mutant of the full-length diphtheria toxin moiety must be used in humans. As discussed throughout the application C-terminal truncation mutants such as, for example, mutants wherein 152, 150, or 145 carboxy terminal amino acids were truncated including DT390, were specifically designed to avoid the anti-diphtheria antibody response. Therefore, the use of UCHT1-DT390 or other C-terminal truncation mutants to inhibit transplant rejection were in Applicants' possession.

Applicants respectfully point out that because kidney transplants were previously considered by the examiner and the use of the UCHT1 antibody makes human subjects an inherent property of the claims, no new issues are raised by these amendments and no new

search is necessary. Applicants believe this rejection to be overcome and respectfully request its withdrawal.

Regarding the rejection of claim 48 under 35 U.S.C. 112, first paragraph, the Examiner alleges that there is a lack of written description support for a "truncated toxin moiety not recognized by inhibitory anti-diphtheria toxin antibodies." Applicants respectfully traverse this rejection. Although Applicants have previously pointed to support for this limitation on page 40, lines 28-32 and page 39, lines 11-14 when claim 48 was introduced, and the claim was adequately described as written, Applicants have again amended claim 48 to track the language of the specification on page 40, lines 28-32 which describes a truncated toxin moiety that bypasses the inhibitory effect of pre-existing anti-diptheria antibodies. Applicants have made this amendment to insure no confusion could exist with respect to description in the specification and believe that the amendment in no way further limits the claims as it is of the exact same scope and merely rephrases as limitation to more closely track the exact wording of the specification. Applicants also note that as this support and this limitation have been previously considered by the Examiner, the amendment raises no new issues.

Regarding the remainder of the claim, Applicants note that, as previously pointed out, original claims 4-7 as well as Applicants' amendment to the specification, which provides literal description in the specification for the original claims as provided in MPEP 2163.06, describe immunotoxins comprising UCHT1 and, generically, a mutant diphtheria toxin moiety. For example, original claim 4 importing the limitations of claim 1 recites "an immunotoxin, comprising a mutant diphtheria toxin moiety linked to a single chain variable region antibody which routes by the anti-CD3 pathway, or derivatives thereof, wherein the antibody comprises the UCHT1 V_LV_H region." Similarly, original claim 5 recites "the immunotoxin of claim 4, wherein the antibody comprises human CH2 and CH3 regions." By importing the limitations of the claims from which claim 5 is dependent, claim 5 recites "an immunotoxin, comprising a mutant diphtheria toxin moiety linked to a single chain variable region antibody which routes by the anti-CD3 pathway, or derivatives thereof, wherein the antibody comprises the UCHT1 V_LV_H region, wherein the antibody comprises human CH2 and CH3 regions." Therefore, Applicants

have support for claim 48 as written in the form of original claims 1 and 4-7, the amendment to the specification provided in Applicants' previous response, as well as on page 39, lines 11-14 and page 40, lines 28-32. Applicants believe this rejection to be overcome and respectfully request its withdrawal.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application are believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

No fee is believed to be due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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J. Gibson Lanier — Date 9/8/06